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Treatment of various substituted semicarbazones of aromatic aldehydes with sulfur monochloride yields the corresponding substituted 2,4-dihydro-1,2,4-triazol-3-ones. With thiosemicarbazones, the products are derivatives either of the 2-amino-1,3,4-thiadiazole or of the 2,4-dihydro-1,2,4-triazole-3-thione depending on the experimental conditions.

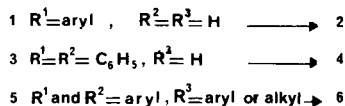
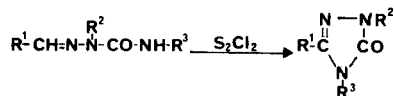
J. Heterocyclic Chem., **23**, 881 (1986).

A few works on the reactions of sulfur monochloride with some nitrogen compounds have been investigated. For example, sulfur monochloride gives aminodisulfides with primary and secondary amines [1,2], diamidosulfides with primary amides [3], the 3,4,7,8-tetramethyl-1,2,5,6-, 3,4,7,8-tetrathiatetrazocine with the 1,2-dimethylhydrazine [4] and a mixture of tetrazans and 1,3,4-oxadiazolines with 2-acyl-1,1-dimethylhydrazines [5].

A proposed mechanism for these last reactions [5] involves *N*- (or *O*)-chlorodithio compounds as intermediates which can either undergo duplication or heterocyclization, depending on the thermodynamic criteria bound to their structure.

In view of these results, we have undertaken reactions of sulfur monochloride with various aldehyde semicarbazones and thiosemicarbazones, with the purpose of finding new methods of syntheses of diverse substituted 2,4-dihydro-1,2,4-triazol-3-ones and 2,4-dihydro-1,2,4-triazole-3-thiones respectively.

Semicarbazones of structures **1**, **3** and **5** in the presence of sulfur monochloride were converted into the corresponding mono, di or trisubstituted 2,4-dihydro-1,2,4-triazol-3-ones **2**, **4** and **6** (Scheme 1).



Scheme 1

The reactions with **1** were carried out in refluxing mixture acetic acid-ethyl acetate (1-4). After 3 or 4 hours, 5-aryl-2,4-dihydro-1,2,4-triazol-3-ones **2** were obtained in good yields (Table 1). However, when the substituent R^1 was a *para*-nitrophenyl group, no reaction occurred.

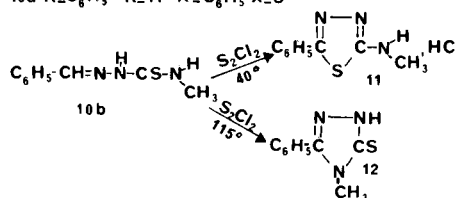
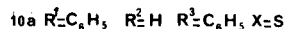
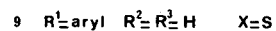
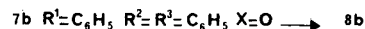
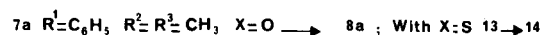
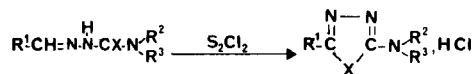
Under the same conditions as above, the semicarbazone

3 was converted into the 2,5-diphenyl-2,4-dihydro-1,2,4-triazol-3-one (**4**) (Table 1). This semicarbazone **3** was obtained from the reaction between ammonia and the benzaldehyde 2-phenyl-2-chloroformylhydrazone [6,7].

A particularly interesting reaction occurred by the action of sulfur monochloride on semicarbazones **5**.

In a previous paper [7], we have proposed a general procedure for the preparation of 2,4,5-trisubstituted 2,4-dihydro-1,2,4-triazol-3-ones **6**. The method consisted of oxidizing a number of semicarbazones **5** with lead dioxide in an aliphatic acid as the medium. Nevertheless, it was limited when the substituent R^3 was an aliphatic one or bore an electron-withdrawing group: no corresponding triazolone **6** was produced. The use of sulfur monochloride afforded those heterocycles **6** in satisfactory yields (Table 1).

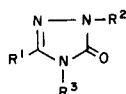
The action of sulfur monochloride on semicarbazones **7a** and **7b** gave mainly resinifications, even at -20° . By analytical chromatography, only traces of the corresponding 2-dimethyl (or diphenyl)amino-5-phenyl-1,3,4-oxadiazoles were observed, respectively (**8a**) and (**8b**) (Scheme II).



Scheme II

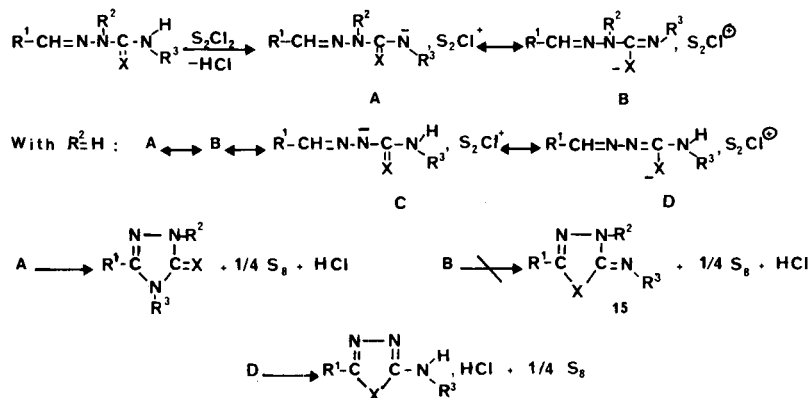
Tarry products were also formed with thiosemicarbazones **9** and **10a**. However, treatment of **10b** with sulfur

Table 1



Compound	R ¹	R ²	R ³	Yield (%)	Mp °C
2a	C ₆ H ₅	H	H	62	323 [a]
2b	4-CH ₃ O-C ₆ H ₄	H	H	64	334 [b]
2c	4-Cl-C ₆ H ₄	H	H	51	380 dec [c]
2d	2-HO-C ₆ H ₄	H	H	70	330 [d]
4	C ₆ H ₅	C ₆ H ₅	H	32	234-236 [e]
6a	C ₆ H ₅	C ₆ H ₅	C ₂ H ₅	52	80
6b	C ₆ H ₅	C ₆ H ₅	<i>n</i> -C ₂ H ₇	54	82
6c	C ₆ H ₅	C ₆ H ₅	<i>n</i> -C ₄ H ₉	68	70
6d	C ₆ H ₅	C ₆ H ₅	C ₆ H ₅	72	221 [f]
6e	C ₆ H ₅	C ₆ H ₅	3-NO ₂ -C ₆ H ₄	68	160
6f	4-CH ₃ -C ₆ H ₄	C ₆ H ₅	2,5-diCl-C ₆ H ₃	81	161-162
6g	4-CH ₃ O-C ₆ H ₄	C ₆ H ₅	C ₆ H ₅	80	174 [13]
6h	4-Cl-C ₆ H ₄	C ₆ H ₅	C ₆ H ₅	68	188 [13]

[a] Lit [8] mp 323-324° dec. [b] Lit [8] mp 334-335° dec. [c] Lit [8] mp >400°. [d] Lit [9] mp 330° dec. [e] Lit [10] mp 229-230°. [f] Lit [11] mp 221.5-222°.



Scheme III

monochloride at 40° in ethyl acetate gave the 2-methyl-amino-5-phenyl-1,3,4-thiadiazole (**11**), in low yield, along with tars. On refluxing in acetic acid for 10 minutes, this reaction afforded the 4-methyl-5-phenyl-2,4-dihydro-1,2,4-triazole-3-thione (**12**) in good yield.

At last, the thiosemicarbazone **13** in acetic acid at room temperature reacted immediately with sulfur monochloride to give the 2-dimethylamino-5-phenyl-1,3,4-thiadiazole (**14**).

According to previous works [5], this pathway would afford *N*-chlorodithio compounds. With semicarbazones or thiosemicarbazones, sulfur monochloride could give an anion which would present two contributing forms **A** and **B** when R² is different from H and four contributing forms

A, **B**, **C** and **D** when R² is an hydrogen (Scheme III).

Cyclization of this anion would provide 1,2,4-triazole-3-one or 1,2,4-triazole-3-thione or also 2-amino-1,3,4-oxadiazole as well as 2-amino-1,3,4-thiadiazole.

The structure **15** which theoretically could also be a result of this reaction has never been obtained.

The chlorination of the starting product by sulfur monochloride yielding an α -chlorobenzaldehyde semicarbazone or thiosemicarbazone and this cyclization could be another possible mechanism. But the speed of some reactions and no appearance of the intermediate by chromatography for the slowest ones are two reasons which permit us to consider that the first proposed mechanism is the most probable.

EXPERIMENTAL

Melting points were taken with a Buchi oil heated apparatus and are uncorrected. The ir spectra were recorded on a Perkin Elmer 1310 spectrophotometer as potassium bromide disks. The ¹H-nmr spectra were obtained on a Varian T-60 spectrometer and are reported as δ values (ppm) relative to tetramethylsilane as an internal standard.

5-Aryl-2,4-dihydro-1,2,4-triazol-3-ones **2a-d** and 2,5-Diphenyl-2,4-dihydro-1,2,4-triazol-3-one (**4**).

A solution of 0.27 g (2 mmoles) of sulfur monochloride and 1 mmole of semicarbazones **1** or **3** in 50 ml of an anhydrous mixture of acetic acid-ethyl acetate (1-4) was refluxed for 3 to 4 hours. After cooling, one part of the target compounds **2a-d** or **4** precipitated and was filtered. The solvent was evaporated *in vacuo* and some additional products mixed up with sulfur were collected. Their purification required several recrystallizations from an appropriate solvent in the presence of reduced copper and activated charcoal.

4-Alkyl-2,5-diphenyl-2,4-dihydro-1,2,4-triazol-3-ones **6a-c**.

To a solution of 0.27 g (2 mmoles) of sulfur monochloride in 10 ml of anhydrous chloroform, were added 2 mmoles of semicarbazones **5a**, **5b** or **5c**. The reaction mixture was stirred at 25° for 12 hours. The mixture was filtered, washed with 10% aqueous sodium bicarbonate and dried over anhydrous sodium sulfate. After removal of the chloroform, the compounds **6a-c** mixed with sulfur were purified by column chromatography on Macherey-Nagel silica gel 60 (0.05-0.2 mm) using dichloromethane as the eluent.

4-Ethyl-2,5-diphenyl-2,4-dihydro-1,2,4-triazol-3-one (**6a**).

This compound had ir: 1700 cm⁻¹ (C=O); nmr (DMSO-d₆): δ 1.2 (t, 3H), 3.85 (q, 2H), 7.2-8.15 (m, 10H).

Anal. Calcd. for C₁₆H₁₅N₃O: C, 72.4; H, 5.7; N, 15.8. Found: C, 72.5; H, 5.7; N, 16.0.

2,5-Diphenyl-4-n-propyl-2,4-dihydro-1,2,4-triazole-3-one (**6b**).

This compound had ir: 1700 cm⁻¹ (C=O); nmr (DMSO-d₆): δ 0.7 (t, 3H), 1.3-1.8 (m, 2H), 3.75 (t, 2H), 7.1-8.1 (m, 10H).

Anal. Calcd. for C₁₇H₁₇N₃O: C, 73.1; H, 6.1; N, 15.0. Found: C, 73.0; H, 6.2; N, 15.1.

4-n-Butyl-2,5-diphenyl-2,4-dihydro-1,2,4-triazol-3-ones (**6c**).

This compound had ir: 1700 cm⁻¹ (C=O); nmr (DMSO-d₆): δ 0.8 (t, 3H), 1.2-1.8 (m, 4H), 3.8 (t, 2H), 7.2-8.15 (m, 10H).

Anal. Calcd. C₁₈H₁₉N₃O: C, 73.7; H, 6.5; N, 14.3. Found: C, 73.7; H, 6.5; N, 14.4.

2,4,5-Triaryl-2,4-dihydro-1,2,4-triazol-3-ones **6d-h**.

An equimolecular solution (1 mmole) of semicarbazones **5d-h** and of 0.135 g of sulfur monochloride in 20 ml of anhydrous acetic acid was refluxed for 15 minutes. The solvent was evaporated *in vacuo* and the products **6** were purified as above, except compound **6e** which was recrystallized from ethanol in the presence of reduced copper.

4-(3-Nitrophenyl)-2,5-diphenyl-2,4-dihydro-1,2,4-triazol-3-one (**6e**).

This compound had ir: 1710 cm⁻¹ (C=O); nmr (DMSO-d₆): δ 7.3-8.5 (m).

Anal. Calcd. for C₂₀H₁₄N₄O₃: C, 67.0; H, 3.9; N, 15.6. Found: C, 67.2; H, 4.1; N, 15.6.

4-(2,5-Dichlorophenyl)-5-(4-methylphenyl)-2-diphenyl-2,4-dihydro-1,2,4-triazol-3-one (**6f**).

This compound had ir: 1720 cm⁻¹ (C=O); nmr (DMSO-d₆): δ 2.35 (s, 3H), 7.2-7.9 (m, 10H), 8.1 (d, 2H).

Anal. Calcd. for C₂₁H₁₅Cl₂N₃O: C, 63.7; H, 3.8; N, 10.6. Found: C, 63.6; H, 3.8; N, 10.5.

2-Methylamino-5-phenyl-1,3,4-thiadiazole (**11**).

To a stirred solution of 1.16 g (6 mmoles) of **10b** in 50 ml of anhydrous ethyl acetate at 40°, was added 0.95 g (7 mmoles) of sulfur monochloride. A white precipitate appeared after 15 minutes. The mixture was then refluxed for 15 minutes. The solid was filtered and dissolved in 10% aqueous sodium bicarbonate. The alkaline solution was extracted with ether. After evaporation of the solvent, the thiadiazole **11** was recrystallized several times from ethanol in the presence of reduced copper, giving 0.11 g (10%) of **11**, mp 184°, lit [13] mp 183-184°.

4-Methyl-5-phenyl-2,4-dihydro-1,2,4-triazole-3-thione (**12**).

To a stirred solution of 1.16 g (6 mmoles) of **10b** in 25 ml of anhydrous acetic acid, was added 0.81 g (6 mmoles) of sulfur monochloride. The mixture was refluxed for 10 minutes, filtered and the solvent removed *in vacuo*. The oily residue was dissolved in 20 ml of 1 N aqueous sodium hydroxide. The solution was filtered and acidified with acetic acid. The precipitate was collected by filtration and recrystallized from ethanol in the presence of reduced copper, giving 0.86 g (75%) of **12**, mp 164°, lit [14] mp 166°.

2-Dimethylamino-5-phenyl-1,3,4-thiadiazole (**14**).

To a solution of 0.83 g (4 mmoles) of **13** in 30 ml of anhydrous acetic acid at room temperature, was added 0.54 g (4 mmoles) of sulfur monochloride. After removal of the acid acetic *in vacuo*, the resulting residue was dissolved in 50 ml of water. The solution was filtered, neutralized with acetic acid and extracted with ether. The organic solution was dried over magnesium sulfate and evaporated. The residue was recrystallized from ether/petroleum ether 40-60 giving 0.41 g (50%) of **14**, mp 98°, lit [15] mp 98°.

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